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•Practice Limited to  
Federal Agencies

September 27, 2004

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Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

*Mail Stop: Amendment*

Re: U.S. Utility Patent Application  
Appl. No.: 10/661,819; Filed: September 15, 2003  
For: **Thermostable Reverse Transcriptases and Uses Thereof**  
Inventors: Michael D. SMITH *et al.*  
Our Ref: 0942.5040003/RWE/HCC

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Information Disclosure Statement Under 37 C.F.R. § 1.97(b);
2. A listing of the cited documents on Form PTO-1449 (*15 pages*);
3. Copies of the cited documents (AI1-AJ1 and AL1-AM15);
4. First Supplemental Information Disclosure Statement Under 37 C.F.R. § 1.97(b);
5. A listing of the cited documents on Form PTO-1449 (*15 pages*);
6. Copies of the cited documents (AL16, AR1-AT1, AR2-AT2, AR3-AT3, AR4-AT4, AR5-AT5, AR6-AT6, AR7-AT7, AR8-AT8, AR9-AT9, AR10-AT10, AR11-AT11, AR12-AT12, AR13-AT13, AR14-AT14 and AR15);
7. Second Supplemental Information Disclosure Statement Under 37 C.F.R. § 1.97(b);
8. A listing of the cited documents on Form PTO-1449 (*2 pages*);
9. Copies of the cited documents (AS15-AT15 and AR16);
10. Third Supplemental Information Disclosure Statement Under 37 C.F.R. § 1.97(b);

Commissioner for Patents  
September 27, 2004  
Page 2

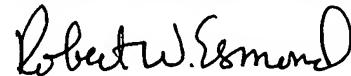
11. A listing of the cited documents on Form PTO-1449 (*3 pages*);
12. Copies of the cited documents (AM16, AS16-AT16, AR17-AT17 and AR18);
13. Fourth Supplemental Information Disclosure Statement Under 37 C.F.R. § 1.97(b);
14. A listing of the cited documents on Form PTO-1449 (*2 pages*);
15. Copies of the cited documents (AS18-AT18 and AR19); and
16. One (1) return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Robert W. Esmond  
Attorney for Applicants  
Registration No. 32,893

RWE/AWL:ddc  
Enclosures

315583\_1.DOC



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Smith *et al.*

Appl. No.: 10/661,819

Filed: September 15, 2003

For: **Thermostable Reverse  
Transcriptases and Uses Thereof**

Confirmation No.: 7510

Art Unit: 1651

Examiner: *To Be Assigned*

Atty. Docket: 0942.5040003/RWE/HCC

**Information Disclosure Statement Under 37 C.F.R. § 1.97(b)**

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. Copies of U.S. patents and patent application publications, AA1 to AG1, cited on the attached Form PTO-1449 are not being submitted in accordance with 1276 OG 55 because this application was filed after June 30, 2003. Copies of documents AI1 to AJ1 and AL1 to AM15 are provided.

The Examiner's attention is directed to the following application:

U.S. Application No. 09/677,574, filed October 3, 2000, pending;

which is directed to related technical subject matter. The identification of this U.S. Patent Application is not to be construed as a waiver if secrecy as to this application now or upon issuance of the present application as a patent. The Examiner is respectfully requested to consider the cited application and the art cited therein during examination.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates

should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

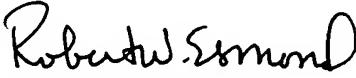
This Information Disclosure Statement is being filed before the mailing of an Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

  
Robert W. Esmond  
Attorney for Applicants  
Registration No. 32,893

Date: Sept. 27, 2004

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INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO. 0942.5040003/RWE/HCC	APPLICATION NO. 10/661,819
		APPLICANT Smith et al.	
		FILING DATE September 15, 2003	GROUP 1651

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA1	5,244,797	09/14/1993	Kotewicz et al.			03/18/1991
	AB1	B1 5,244,797	08/25/1998	Kotewicz et al.			03/18/1991
	AC1	5,405,776	04/11/1995	Kotewicz et al.			01/24/1992
	AD1	B1 5,405,776	10/01/1996	Kotewicz et al.			01/24/1992
	AE1	5,668,005	09/16/1997	Kotewicz et al.			03/12/1996
	AF1	6,063,608	05/16/2000	Kotewicz et al.			02/10/1997
	AG1	6,136,582	10/24/2000	Gao et al.			01/20/1998
	AH						

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AI1	WO 98/47912	10/29/1998	WIPO			Yes No
	AJ1	WO 99/10366	03/04/1999	WIPO			Yes No
	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	1	Arion, D., et al., "The K65R Mutation Confers Increased DNA Polymerase Processivity to HIV-1 Reverse Transcriptase," <i>J. Biol. Chem.</i> 271:19860-19864, American Society for Biochemistry and Molecular Biology (1996)
	AM	1	Bakhanashvili, M., and Hizi, A., "The fidelity of the reverse transcriptases of human immunodeficiency viruses and murine leukemia virus, exhibited by the mispair extension frequencies, is sequence dependent and enzyme related," <i>FEBS</i> 319:201-205, Elsevier Science Publishers B.V. (1993)
	AN	1	Bakhanashvili, M., and Hizi, A., "A possible role for cysteine residues in the fidelity of DNA synthesis exhibited by the reverse transcriptases of human immunodeficiency viruses type 1 and type 2," <i>FEBS</i> 304:289-293, Elsevier Science Publishers B.V. (1992)
	AO	1	Bakhanashvili, M., et al., "Mutational studies of human immunodeficiency virus type 1 reverse transcriptase: the involvement of residues 183 and 184 in the fidelity of DNA synthesis," <i>FEBS Lett.</i> 391:257-262, Elsevier Science Publishers B.V. (1996)
	AP	1	Bakhanashvili, M., and Hizi, A., "Fidelity of the RNA-Dependent DNA Synthesis Exhibited by the Reverse Transcriptases of Human Immunodeficiency Virus Types 1 and 2 and of Murine Leukemia Virus: Mispair Extension Frequencies," <i>Biochem.</i> 31:9393-9398, American Chemical Society (1992)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.



FORM PTO-1449

INFORMATION DISCLOSURE STATEMENTATTY. DOCKET NO.  
0942.5040003/RWE/HCCAPPLICATION NO.  
10/661,819APPLICANT  
Smith et al.FILING DATE  
September 15, 2003GROUP  
1651**U.S. PATENT DOCUMENTS**

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
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**FOREIGN PATENT DOCUMENTS**

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	AI						Yes No
	AJ						Yes No
	AK						Yes No

**OTHER (Including Author, Title, Date, Pertinent Pages, etc.)**

	AL	2	Barnes, W.M., "The fidelity of Tag polymerase catalyzing PCR is improved by an N-terminal deletion," <i>Gene</i> 112:29-35, Elsevier Science Publishers B.V. (1992)
	AM	2	Basu, S., et al., "Sulphydryl groups in the template-primer-binding domain of murine leukemia virus reverse transcriptase," <i>Biochem. J.</i> 296:577-583, The Chemical Society, London (1993)
	AN	2	Bebenek, K., et al., "Reduced Frameshift Fidelity and Processivity of HIV-1 Reverse Transcriptase Mutants Containing Alanine Substitutions in Helix H of the Thumb Subdomain," <i>J. Biol. Chem.</i> 270:19516-19523, American Society for Biochemistry and Molecular Biology (1995)
	AO	2	Bebenek, K., et al., "The Fidelity of DNA Synthesis Catalyzed by Derivatives of <i>Escherichia coli</i> DNA Polymerase I," <i>J. Biol. Chem.</i> 265:13878-13887, The American Society for Biochemistry and Molecular Biology (1990)
	AP	2	Ben-Artzi, H., et al., "Characterization of the double stranded RNA dependent RNase activity associated with recombinant reverse transcriptases," <i>Nucleic Acids Res.</i> 20:5115-5118, Oxford University Press (1992)

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			APPLICANT Smith et al.			
			FILING DATE September 15, 2003		GROUP 1651	

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	AI						Yes No
	AJ						Yes No
	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AL	<u>3</u>	Berger, S.L., et al., "Reverse Transcriptase and Its Associated Ribonuclease H: Interplay of Two Enzyme Activities Controls the Yield of Single-Stranded Complementary Deoxyribonucleic Acid," <i>Biochemistry</i> 22:2365-2372, The American Chemical Society (1983)
AM	<u>3</u>	Blain, S.W., and Goff, S.P., "Effects on DNA Synthesis and Translocation Caused by Mutations in the RNase H Domain of Moloney Murine Leukemia Virus Reverse Transcriptase," <i>J. Virol.</i> 69:4440-4452, The American Society for Microbiology (1995)
AN	<u>3</u>	Caliendo, A.M., et al., "Effects of Zidovudine-Selected Human Immunodeficiency Virus Type 1 Reverse Transcriptase Amino Acid Substitutions on Processive DNA Synthesis and Viral Replication," <i>J. Virol.</i> 70:2146-2153, The American Society for Microbiology (1996)
AO	<u>3</u>	Carroll, S.S., et al., "A Mutant of DNA Polymerase I (Klenow Fragment) with Reduced Fidelity," <i>Biochem.</i> 30:804-813, American Chemical Society (1991)
AP	<u>3</u>	Carter, P. and Wells, J.A., "Engineering Enzyme Specificity by 'Substrate-Assisted Catalysis,'" <i>Science</i> 237:394-399, American Association for the Advancement of Science (1987)

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	AI						Yes No
	AJ						Yes No
	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	4	Chen, Y., and Marion, P.L., "Amino Acids Essential for RNase H Activity of Hepadnaviruses Are Also Required for Efficient Elongation of Minus-Strand Viral DNA," <i>J. Virol.</i> 70:6151-6156, The American Society for Microbiology (1996)
	AM	4	Chowdhury, K., et al., "Elucidation of the Role of Arg 110 of Murine Leukemia Virus Reverse Transcriptase in the Catalytic Mechanism: Biochemical Characterization of Its Mutant Enzymes," <i>Biochemistry</i> 35:16610-16620, American Chemical Society (1996)
	AN	4	Creighton, S., et al., "Base Mispair Extension Kinetics," <i>J. Biol. Chem.</i> 267:2633-2639, American Society for Biochemistry and Molecular Biology (1992)
	AO	4	DeStefano, J.J., et al., "Parameters that influence processive synthesis and site-specific termination by human immunodeficiency virus reverse transcriptase on RNA and DNA templates," <i>Biochimica et Biophysica Acta</i> 1131:270-280, Elsevier Science Publishers B.V. (1992)
	AP	4	Diaz, L., and DeStefano, J.J., "Strand transfer is enhanced by mismatched nucleotide at the 3' primer terminus: a possible link between HIV reverse transcriptase fidelity and recombination," <i>Nucleic Acids Res.</i> 24:3086-3092, Oxford University Press (1996)

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	AI						Yes No
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	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	5	Drosopoulos, W.C., and Prasad, V.R., "Increased Polymerase Fidelity of E89G, a Nucleoside Analog-Resistant Variant of Human Immunodeficiency Virus Type 1 Reverse Transcriptase," <i>J. Virol.</i> 70:4834-4838, The American Society for Microbiology (1996)
	AM	5	Drosopoulos, W.C., and Prasad, V.R., "Increased Misincorporation Fidelity Observed for Nucleoside Analog Resistance Mutations M184V and E89G in Human Immunodeficiency Virus Type 1 Reverse Transcriptase Does Not Correlate with the Overall Error Rate Measured In Vitro," <i>J. Virol.</i> 72:4224-4230, The American Society for Microbiology (1998)
	AN	5	Eckert, K.A., and Kunkel, T.A., "Fidelity of DNA synthesis catalyzed by human DNA polymerase $\alpha$ and HIV-1 reverse transcriptase: effect of reaction pH," <i>Nucleic Acids Res.</i> 21:5212-5220, Oxford University Press (1993)
	AO	5	Eger, B.T., et al., "Mechanism of DNA Replication Fidelity for Three Mutants of DNA Polymerase I: Klenow fragment KF(exo+), KF(polA5), and KF(exo-)," <i>Biochem.</i> 30:1441-1448, American Chemical Society (1991)
	AP	5	Feng, J.Y., and Anderson, K.S., "Mechanistic Studies Examining the Efficiency and Fidelity of DNA Synthesis by the 3TC-Resistant Mutant (184V) of HIV-1 Reverse Transcriptase," <i>Biochemistry</i> 38:9440-9448, The American Chemical Society (1999); Published on the web on June 30, 1999.

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	AI						Yes No
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	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AL	6	Finston, W.I. and Champoux, J.J., "RNA-Primed Initiation of Moloney Murine Leukemia Virus Plus Strands by Reverse Transcriptase In Vitro," <i>J. Virology</i> 51:26-33, American Society for Microbiology (1984)
AM	6	Gao, G., and Goff, S.P., "Replication Defect of Moloney Murine Leukemia Virus with a Mutant Reverse Transcriptase That Can Incorporate Ribonucleotides and Deoxyribonucleotides," <i>J. Virol.</i> 72:5905-5911, The American Society for Microbiology (1998)
AN	6	Gerard, G.F., et al., "cDNA Synthesis by Cloned Moloney Murine Leukemia Virus Reverse Transcriptase Lacking RNase H Activity," <i>Focus</i> 11:66-69, Life Technologies, Inc. (1989)
AO	6	Gerard, G.F., et al., "Influence on Stability in <i>Escherichia coli</i> of the Carboxy-Terminal Structure of Cloned Moloney Murine Leukemia Virus Reverse Transcriptase," <i>DNA</i> 5:271-279, Mary Ann Liebert, Inc. (1986)
AP	6	Gerard, G., et al., "cDNA Synthesis by Moloney Murine Leukemia Virus RNase H-Minus Reverse Transcriptase Possessing Full DNA Polymerase Activity," <i>Focus</i> 14:91-93, Life Technologies, Inc. (1992)

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	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	7	Gerwin, B.I., et al., "Mutant of B-Tropic Murine Leukemia Virus Synthesizing an Altered Polymerase Molecule," <i>J. Virology</i> 31:741-751, The American Society for Microbiology (1979)
	AM	7	Goff, S.P., "Retroviral Reverse Transcriptase: Synthesis, Structure, and Function," <i>J. Acquired Immune Deficiency Syndrome</i> 3:817-831, Raven Press (1990)
	AN	7	Goff, S.P. and Lobel, L.I., "Mutants of murine leukemia viruses and retroviral replication," <i>Biochimica et Biophysica Acta</i> . 907:93-123, Elsevier Science Publishers B.V. (1987)
	AO	7	Goobar-Larsson, L., et al., "Disruption of a Salt Bridge between Asp 488 and Lys 465 in HIV-1 Reverse Transcriptase Alters Its Proteolytic Processing and Polymerase Activity," <i>Virology</i> 196:731-738, Academic Press (1993)
	AP	7	Götte, M., et al., "The M184V Mutation in the Reverse Transcriptase of Human Immunodeficiency Virus Type 1 Impairs Rescue of Chain-Terminated DNA Synthesis," <i>J. Virol.</i> 74:3579-3585, The American Society for Microbiology (2000)

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AL	8	Guo, J., et al., "Defects in Primer-Template Binding, Processive DNA Synthesis, and RNase H Activity Associated with Chimeric Reverse Transcriptases Having the Murine Leukemia Virus Polymerase Domain Joined to <i>Escherichia coli</i> RNase H," <i>Biochemistry</i> 34:5018-5029, The American Chemical Society (1995)
AM	8	Hamburgh, M.E., et al., "The influence of 3TC-resistance mutations E89G and M184V in the human immunodeficiency virus reverse transcriptase on mispair extension efficiency," <i>Nucleic Acids Res.</i> 26:4389-4394, Oxford University Press (1998)
AN	8	Hite, J.M., et al., "Factors affecting fidelity of DNA synthesis during PCR amplification of d(C-A) <sub>n</sub> ·d(G-T) <sub>n</sub> microsatellite repeats," <i>Nucleic Acids Res.</i> 24:2429-2434, Oxford University Press (1996)
AO	8	Hsu, M., et al., "Higher fidelity of RNA-dependent DNA mispair extension by M184V drug-resistant than wild-type reverse transcriptase of human immunodeficiency virus type 1," <i>Nucleic Acids Research</i> 25:4532-4536, Oxford University Press (1997)
AP	8	Jin, J., et al., "Analysis of the Role of Glutamine 190 in the Catalytic Mechanism of Murine Leukemia Virus Reverse Transcriptase," <i>J. Biol. Chem.</i> 274:20861-20868, American Society for Biochemistry and Molecular Biology (1999)

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FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>			ATTY. DOCKET NO. 0942.5040003/RWE/HCC	APPLICATION NO. 10/661,819
			APPLICANT Smith et al.	
			FILING DATE September 15, 2003	GROUP 1651

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	AI						Yes No
	AJ						Yes No
	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	9	Kaushik, N., et al., "Role of Glutamine-151 of Human Immunodeficiency Virus Type-1 Reverse Transcriptase in RNA-Directed DNA Synthesis," <i>Biochemistry</i> 36:14430-14438, The American Chemical Society (1997)
	AM	9	Kaushik, N., et al., "Role of Glutamine 151 of Human Immunodeficiency Virus Type-1 Reverse Transcriptase in Substrate Selection As Assessed by Site-Directed Mutagensis," <i>Biochemistry</i> 39:2912-2920, The American Chemical Society (2000); Published on the web on February 22, 2000.
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	AO	9	Kerr, S.G., and Anderson, K.S., "RNA Dependent DNA Replication Fidelity of HIV-1 Reverse Transcriptase: Evidence of Discrimination between DNA and RNA Substrates," <i>Biochemistry</i> 36:14056-14063, The American Chemical Society (1997)
	AP	9	Kim, B., et al., "Fidelity of Mutant HIV-1 Reverse Transcriptases: Interaction with the Single-Stranded Template Influences the Accuracy of DNA Synthesis," <i>Biochemistry</i> 37:5831-5839, The American Chemical Society (1998); Published on the web on April 9, 1998.

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	<u>10</u>	Kim, B., et al., "New Human Immunodeficiency Virus, Type 1 Reverse Transcriptase (HIV-1 RT) Mutants with Increased Fidelity of DNA Synthesis," <i>J. Biol. Chem.</i> 274:27666-27673, American Society for Biochemistry and Molecular Biology (1999)
	AM	<u>10</u>	Levin, J.G., et al., "Murine Leukemia Virus Mutant with a Frameshift in the Reverse Transcriptase Coding Region: Implications for pol Gene Structure," <i>J. Virology</i> 51:470-478, American Society for Microbiology (1984)
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	AL	<u>11</u>	Messer, L.I., et al., "Functional Analysis of Reverse Transcription by a Frameshift pol Mutant of Murine Leukemia Virus," <i>Virology</i> 146:146-152, Academic Press, Inc. (1985)
	AM	<u>11</u>	Oude Essink, B.B., et al., "Increased polymerase fidelity of the 3TC-resistant variants of HIV-1 reverse transcriptase," <i>Nucleic Acids Res.</i> 25:3212-3217, Oxford University Press (1997)
	AN	<u>11</u>	Pandey, V.N., et al., "Role of Methionine 184 of Human Immunodeficiency Virus Type-1 Reverse Transcriptase in the Polymerase Function and Fidelity of DNA Synthesis," <i>Biochemistry</i> 35:2168-2179, The American Chemical Society (1996)
	AO	<u>11</u>	Patel, P.H., et al., "Insights into DNA Polymerization Mechanisms from Structure and Function Analysis of HIV-1 Reverse Transcriptase," <i>Biochemistry</i> 34:5351-5363, The American Chemical Society (1995)
	AP	<u>11</u>	Perrino, F.W., et al., "Extension of mismatched 3' termini of DNA is a major determinant of the infidelity of human immunodeficiency virus type 1 reverse transcriptase," <i>Proc. Natl. Acad. Sci. USA</i> 86:8343-8347, The National Academy of Sciences of the USA (1989)

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	AL	<u>12</u>	Pop, M.P., and Biebricher, C.K., "Kinetic Analysis of Pausing and Fidelity of Human Immunodeficiency Virus Type 1 Reverse Transcription," <i>Biochemistry</i> 35:5054-5062, The American Chemical Society (1996)
	AM	<u>12</u>	Prasad, V.R. and Goff, S.P., "Linker insertion mutagenesis of the human immunodeficiency virus reverse transcriptase expressed in bacteria: Definition of the minimal polymerase domain," <i>Proc. Natl. Acad. Sci. USA</i> 86:3104-3108, The National Academy of Sciences of the USA (1989)
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	AO	<u>12</u>	Repaske, R., et al., "Inhibition of RNase H Activity and Viral Replication by Single Mutations in the 3' Region of Moloney Murine Leukemia Virus Reverse Transcriptase," <i>J. Virology</i> 63:1460-1464, American Society for Microbiology (1989)
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	AL	<u>13</u>	Rezende, L.F., et al., "The Impact of Multidideoxynucleoside Resistance-Conferred Mutations in Human Immunodeficiency Virus Type 1 Reverse Transcriptase on Polymerase Fidelity and Error Specificity," <i>J. Virol.</i> 72:2890-2895, The American Society for Microbiology (1998)
	AM	<u>13</u>	Rezende, L.F., et al., "The influence of 3TC resistance mutation M184I on the fidelity and error specificity of human immunodeficiency virus type 1 reverse transcriptase," <i>Nucleic Acids Res.</i> 26:3066-3072, Oxford University Press (1998)
	AN	<u>13</u>	Rubinek, T., et al., "The fidelity of 3' misinsertion and mispair extension during DNA synthesis exhibited by two drug-resistant mutants of the reverse transcriptase of human immunodeficiency virus type 1 with Leu74→Val and Glu89→Gly," <i>Eur. J. Biochem.</i> 247:238-247, FEBS (1997)
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	AP	<u>13</u>	Sooknanan, R., et al., "Fidelity of Nucleic Acid Amplification with Avian Myeloblastosis Virus Reverse Transcriptase and T7 RNA Polymerase," <i>BioTechniques</i> 17:1077-1080, 1083-1085, Eaton Publishing Co (1994)

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AL	<u>14</u>	Suzuki, M., et al., "Low Fidelity Mutants in the O-Helix of <i>Thermus aquaticus</i> DNA Polymerase I," <i>J. Biol. Chem.</i> 272:11228-11235, The American Society for Biochemistry and Molecular Biology, Inc. (1997)
AM	<u>14</u>	Suzuki, M., et al., "Fidelity Mutants in <i>Thermus aquaticus</i> DNA Polymerase I," <i>Ninth International Genome Sequencing and Analysis Conference, Hilton Head Island, South Carolina, September 13-16, 1997. Microbial and Comparative Genomics</i> 2:226, Abstract C-30, Mary Ann Liebert, Inc. (1997)
AN	<u>14</u>	Taube, R., et al., "The fidelity of misinsertion and mispair extension throughout DNA synthesis exhibited by mutants of the reverse transcriptase of human immunodeficiency virus type 2 resistant to nucleoside analogs," <i>Eur. J. Biochem.</i> 250:106-114, FEBS (1997)
AO	<u>14</u>	Telesnitsky, A. and Goff, S.P., "RNase H domain mutations affect the interaction between Moloney murine leukemia virus reverse transcriptase and its primer-template," <i>Proc. Natl. Acad. Sci. USA</i> 90:1276-1280, The National Academy of Sciences of the USA (1993)
AP	<u>14</u>	Varela-Echavarria, A., et al., "Comparison of Moloney Murine Leukemia Virus Mutation Rate with the Fidelity of Its Reverse Transcriptase in Vitro," <i>J. Biol. Chem.</i> 267:24681-24688, American Society for Biochemistry and Molecular Biology (1992)

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	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	<u>15</u>	Wainberg, M.A., et al., "Enhanced Fidelity of 3TC-Selected Mutant HIV-1 Reverse Transcriptase," <i>Science</i> 271:1282-1285, American Association for the Advancement of Science (1996)				
	AM	<u>15</u>	Co-Pending U.S. Patent Application No. 09/677,574, filed October 3, 2000.				
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Smith *et al.*

Appl. No.: 10/661,819

Filed: September 15, 2003

For: Thermostable Reverse  
Transcriptases and Uses Thereof

Confirmation No.: 7510

Art Unit: 1651

Examiner: *To Be Assigned*

Atty. Docket: 0942.5040003/RWE/HCC

**First Supplemental Information Disclosure Statement**

**Under 37 C.F.R. § 1.97(b)**

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. This First Supplemental Information Disclosure Statement is a continuation of Applicants' Information Disclosure Statement filed herewith in connection with the above-captioned application. Copies of the documents are provided.

In accordance with 37 C.F.R. § 1.98(a)(3), Applicants' undersigned representative submits the following discussion of the relevance of the non-English language document **AL16** cited on Form PTO 1449:

Document **AL16** is in the Japanese language. An unverified English language translation of document AL16 is submitted in the Second Supplemental Information Disclosure Statement as document **AR16**, filed concurrently herewith.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates

should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

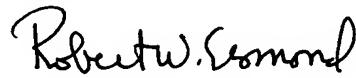
This Information Disclosure Statement is being filed before the mailing of an Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Robert W. Esmond  
Attorney for Applicants  
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Date: Sept. 27, 2004

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	AL16	JP 2000-139457	05/23/2000	Japan			Yes <input checked="" type="checkbox"/> No
	AM						Yes <input type="checkbox"/> No
	AN						Yes <input type="checkbox"/> No
	AO						Yes <input type="checkbox"/> No
	AP						Yes <input type="checkbox"/> No

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	AR	<u>1</u>	Arnold, F.H., et al., "How enzymes adapt: lessons from directed evolution," <i>TRENDS Biochem. Sci.</i> 26:100-106, Elsevier Science Ltd. (February 2001)
	AS	<u>1</u>	Bailey, J.M., "Interpretation of Nitrocellulose Filter Assays of Protein-Nucleic Acid Binding," <i>Anal. Biochem.</i> 93:204-206, Academic Press, Inc. (1979)
	AT	<u>1</u>	Beard, W.A., et al., "Vertical-scanning Mutagenesis of a Critical Tryptophan in the Minor Groove Binding Track of HIV-1 Reverse Transcriptase. Molecular Nature of Polymerase-Nucleic Acid Interaction," <i>J. Biol. Chem.</i> 273:30435-30442, The American Society for Biochemistry and Molecular Biology, Inc. (1998)

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AR	2	Bebenek, K., and Kunkel, T.A., "5. The Fidelity of Retroviral Reverse Transcriptases," in <i>Reverse Transcriptase</i> , Skalka, A.M. and Goff, S.P., eds., Cold Spring Harbor Laboratory Press, Plainview, New York, pp. 85-102 (1993)
AS	2	Bebenek, K., et al., "A minor groove binding track in reverse transcriptase," <i>Nat. Struct. Biol.</i> 4:194-197, Nature Publishing Co. (1997)
AT	2	Cadwell, R.C., and Joyce, G.F., "Randomization of Genes by PCR Mutagenesis," <i>PCR Meth. Appl.</i> 2:28-33, Cold Spring Harbor Laboratory Press (1992)

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AR	3	Cambillau, C., and Claverie, J.-M., "Structural and Genomic Correlates of Hyperthermostability," <i>J. Biol. Chem.</i> 275:32383-32386, The American Society for Biochemistry and Molecular Biology, Inc. (2000)
AS	3	D'Alessio, J.M., and Gerard, G.F., "Second-strand cDNA synthesis with <i>E. coli</i> DNA polymerase I and RNase H: the fate of information at the mRNA 5' terminus and the effect of <i>E. coli</i> DNA ligase," <i>Nucl. Acids Res.</i> 16:1999-2014, IRL Press Ltd. (1988)
AT	3	DeStefano, J.J., et al., "Polymerization and RNase H Activities of the Reverse Transcriptases from Avian Myeloblastosis, Human Immunodeficiency, and Moloney Murine Leukemia Viruses Are Functionally Uncoupled," <i>J. Biol. Chem.</i> 266:7423-7431, The American Society for Biochemistry and Molecular Biology, Inc. (1991)

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	AR	4		DeStefano, J.J., et al., "Characterization of an RNase H deficient mutant of human immunodeficiency virus-1 reverse transcriptase having an aspartate to asparagine change at position 498," <i>Biochim. Biophys. Acta</i> 1219:380-388, Elsevier Science B.V. (1994)			
	AS	4		Ding, J., et al., "Structure and Functional Implications of the Polymerase Active Site Region in a Complex of HIV-1 RT with a Double-stranded DNA Template-primer and an Antibody Fab Fragment at 2.8 Å Resolution," <i>J. Mol. Biol.</i> 284:1095-1111, Academic Press, Inc. (1998)			
	AT	4		Georgiadis, M.M., et al., "Mechanistic implications from the structure of a catalytic fragment of Moloney murine leukemia virus reverse transcriptase," <i>Structure</i> 3:879-892, Current Biology Ltd. (1995)			

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FORM PTO-1449 <b>FIRST SUPPLEMENTAL</b> <b>INFORMATION DISCLOSURE STATEMENT</b>		ATTY. DOCKET NO. 0942.5040003/RWE/HCC		APPLICATION NO. 10/661,819	
		APPLICANT Smith et al.			
		FILING DATE September 15, 2003		GROUP 1651	

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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
AR	5	Gerard, G.F., et al., "Poly(2'-O-methylcytidylate) Oligodeoxyguanylate as a Template for the Ribonucleic Acid Directed Deoxyribonucleic Acid Polymerase in Ribonucleic Acid Tumor Virus Particles and a Specific Probe for the Ribonucleic Acid Directed Enzyme in Transformed Murine Cells," <i>Biochem.</i> 13:1632-1641, The American Chemical Society (1974)					
AS	5	Gerard, G.F., and D'Alessio, J.M., "Reverse Transcriptase (EC 2.7.7.49). The Use of Cloned Moloney Murine Leukemia Virus Reverse Transcriptase to Synthesize DNA from RNA," in <i>Methods in Molecular Biology</i> , Volume 16: <i>Enzymes of Molecular Biology</i> , Burrell, M.M., ed., Humana Press, Totowa, NJ, pp.73-93 (1993)					
AT	5	Gerard, G.F., et al., "Reverse Transcriptase. The Use of Cloned Moloney Murine Leukemia Virus Reverse Transcriptase to Synthesize DNA from RNA," <i>Mol. Biotechnol.</i> 8:61-77, Humana Press (1997)					

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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>6</u>	Harrison, G.P., et al., "Pausing of reverse transcriptase on retroviral RNA templates is influenced by secondary structures both 5' and 3' of the catalytic site," <i>Nucl. Acids Res.</i> 26:3433-3442, Oxford University Press (1998)
AS	<u>6</u>	Houts, G.E., et al., "Reverse Transcriptase from Avian Myeloblastosis Virus," <i>J. Virol.</i> 29:517-522, American Society for Microbiology (1979)
AT	<u>6</u>	Huang, H., et al., "Structure of a Covalently Trapped Catalytic Complex of HIV-1 Reverse Transcriptase: Implications for Drug Resistance," <i>Science</i> 282:1669-1675, American Association for the Advancement of Science (1998)

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	7	Jacobo-Molina, A., et al., "Crystal structure of human immunodeficiency virus type 1 reverse transcriptase complexed with double-stranded DNA at 3.0 Å resolution shows bent DNA," <i>Proc. Natl. Acad. Sci. (USA)</i> 90:6320-6324, National Academy of Sciences of the USA (1993)				
	AS	7	Kohlstaedt, L.A., et al., "Crystal Structure at 3.5 Å Resolution of HIV-1 Reverse Transcriptase Complexed with an Inhibitor," <i>Science</i> 256:1783-1790, American Association for the Advancement of Science (1992)				
	AT	7	Kotewicz, M.L., et al., "Isolation of cloned Moloney murine leukemia virus reverse transcriptase lacking ribonuclease H activity," <i>Nucl. Acids Res.</i> 16:265-277, IRL Press Ltd. (1988)				

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AR	8	Kneller, D.G., et al., "Improvements in Protein Secondary Structure Prediction by An Enhanced Neural Network," <i>J. Mol. Biol.</i> 214:171-182, Academic Press Ltd. (1990)					
AS	8	Krug, M.S., and Berger, S.L., "[33] First-Strand cDNA Synthesis Primed with Oligo(dT)," <i>Meth. Enzymol.</i> 152:316-325, Academic Press, Inc. (1987)					
AT	8	Kumar, S., and Nussinov, R., "How do thermophilic proteins deal with heat?" <i>Cell. Mol. Life Sci.</i> 58:1216-1233, Birkhauser Verlag (August 2001)					

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	9	Kunkel, T.A., et al., "[19] Rapid and Efficient Site-Specific Mutagenesis without Phenotypic Selection," <i>Meth. Enzymol.</i> 154:367-383, Academic Press, Inc. (1987)
AS	9	Kunkel, T.A., et al., "[6] Efficient Site-Directed Mutagenesis Using Uracil-Containing DNA," <i>Meth. Enzymol.</i> 204:125-139, Academic Press, Inc. (1991)
AT	9	Le Grice, S.F.J., "9. Human Immunodeficiency Virus Reverse Transcriptase," in <i>Reverse Transcriptase</i> , Skalka, A.M. and Goff, S.P., eds., Cold Spring Harbor Laboratory Press, Plainview, NY, pp. 163-191 (1993)

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	10	Lehmann, M., and Wyss, M., "Engineering proteins for thermostability: the use of sequence alignments versus rational design and directed evolution," <i>Curr. Opin. Biotechnol.</i> 12:371-375, Elsevier Science Ltd. (August 2001)				
	AS	10	Leung, D.W., et al., "A Method for Random Mutagenesis of a Defined DNA Segment Using a Modified Polymerase Chain Reaction," <i>Technique</i> 1:11-15, W.B. Saunders Co. (1989)				
	AT	10	McDonell, M.W., et al., "Analysis of Restriction Fragments of T7 DNA and Determination of Molecular Weights by Electrophoresis in Neutral and Alkaline Gels," <i>J. Mol. Biol.</i> 110:119-146, Academic Press, Inc. (1977)				

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	AR	<u>11</u>	Mölling, K., et al., "Association of Viral Reverse Transcriptase with an Enzyme degrading the RNA Moiety of RNA-DNA Hybrids," <i>Nature New Biology</i> 234:240-243, Macmillan Journals Ltd. (1971)				
	AS	<u>11</u>	Myers, T.W., and Gelfand, D.H., "Reverse Transcription and DNA Amplification by a <i>Thermus thermophilus</i> DNA Polymerase," <i>Biochem</i> 30:7661-7666, The American Chemical Society (1991)				
	AT	<u>11</u>	Polesky, A.H., et al., "Identification of Residues Critical for the Polymerase Activity of the Klenow Fragment of DNA Polymerase I from <i>Escherichia coli</i> ," <i>J. Biol. Chem.</i> 265:14579-14591, The American Society for Biochemistry and Molecular Biology, Inc. (1990)				

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	<u>12</u>	Prasad, V.R., "8. Genetic Analysis of Retroviral Reverse Transcriptase Structure and Function," in <i>Reverse Transcriptase</i> , Skalka, A.M. and Goff, S.P., eds., Cold Spring Harbor Laboratory Press, Plainview, NY, pp. 135-162 (1993)				
	AS	<u>12</u>	Rost, B., "[31] PHD: Predicting One-Dimensional Protein Structure by Profile-Based Neural Networks," <i>Meth. Enzymol.</i> 266:525-539, Academic Press, Inc. (1996)				
	AT	<u>12</u>	Shinnick, T.M., et al., "Nucleotide sequence of Moloney murine leukaemia virus," <i>Nature</i> 293:543-548, Macmillan Journals Ltd. (1981)				

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)								
	AR	<u>13</u>	Skalka, A.M., "10. Endonuclease Activity Associated with Reverse Transcriptase of Avian Sarcoma-Leukosis Viruses," in <i>Reverse Transcriptase</i> , Skalka, A.M. and Goff, S.P., eds., Cold Spring Harbor Laboratory Press, Plainview, NY, pp. 193-204 (1993)					
	AS	<u>13</u>	Stemmer, W.P.C., "Rapid evolution of a protein in vitro by DNA shuffling," <i>Nature</i> 370:389-391, Macmillan Journals Ltd. (1994)					
	AT	<u>13</u>	Strauss, H.S., et al., "Variables affecting the selectivity and efficiency of retention of DNA fragments by <i>E. coli</i> RNA polymerase in the nitrocellulose-filter-binding assay," <i>Gene</i> 13:75-87, Elsevier/North-Holland Biomedical Press (1981)					

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AR	<u>14</u>	Tosh, C., et al., "One-Tube and One-Buffer System of RT-PCR Amplification of 1D Gene of Foot-and-Mouth Disease Virus Field Isolates," <i>Acta Virol.</i> 41:153-155, Slovak Academic Press (1997)					
AS	<u>14</u>	Verma, I., et al., "Studies on Reverse Transcriptase of RNA Tumor Viruses. III. Properties of Purified Moloney Murine Leukemia Virus DNA Polymerase and Associated RNase H," <i>J. Virol.</i> 15:843-854, American Society for Microbiology (1975)					
AT	<u>14</u>	Wells, J.A., "Additivity of Mutational Effects in Proteins," <i>Biochem.</i> 29:8509-8517, The American Chemical Society (1990)					

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AR	15			Wu, W., et al., "Human Immunodeficiency Virus Type 1 Nucleocapsid Protein Reduces Reverse Transcriptase Pausing at a Secondary Structure near the Murine Leukemia Virus Polypurine Tract," <i>J. Virol.</i> 70:7132-7142, American Society for Microbiology (1996)			
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Smith *et al.*

Appl. No.: 10/661,819

Filed: September 15, 2003

For: **Thermostable Reverse  
Transcriptases and Uses Thereof**

Confirmation No.: 7510

Art Unit: 1651

Examiner: *To Be Assigned*

Atty. Docket: 0942.5040003/RWE/HCC

**Second Supplemental Information Disclosure Statement**

**Under 37 C.F.R. § 1.97(b)**

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. The numbering on this Second Supplemental Information Disclosure Statement is a continuation of the numbering in Applicants' First Supplemental Information Disclosure Statement filed herewith in connection with the above-captioned application. Copies of documents are provided.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

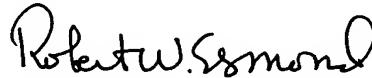
This Information Disclosure Statement is being filed before the mailing of an Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Robert W. Esmond  
Attorney for Applicants  
Registration No. 32,893

Date: Sept. 27, 2004

1100 New York Avenue, N.W.  
Washington, D.C. 20005-3934  
(202) 371-2600

FORM PTO-1449

SECOND SUPPLEMENTAL INFORMATION DISCLOSURE  
STATEMENTATTY. DOCKET NO.  
0942.5040003/RWE/HCCAPPLICATION NO.  
10/661,819FIRST NAMED INVENTOR  
Smith et al.FILING DATE  
September 15, 2003ART UNIT  
1651**U.S. PATENT DOCUMENTS**

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	AR		
	AS	15	Halvas, E.K., et al., "Development of an In Vivo Assay to Identify Structural Determinants in Murine Leukemia Reverse Transcriptase Important for Fidelity," <i>J. Virol.</i> 74:312-319, American Society for Microbiology (January 2000)
	AT	15	Kaushik, N., et al., "Valine of the YVDD Motif of Moloney Murine Leukemia Virus Reverse Transcriptase: Role in the Fidelity of DNA Synthesis," <i>Biochemistry</i> 39:5155-5165, American Chemical Society (May 2000), published on the Web 04/07/2000

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<u>SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT</u>		FIRST NAMED INVENTOR <i>Smith et al.</i>	
		FILING DATE September 15, 2003	ART UNIT 1651

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FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

**OTHER (Including Author, Title, Date, Pertinent Pages, etc.)**

AR	16	Unverified English language translation of JP 2000-139457, Ralph McElroy Translation Company
AS		
AT		

EXAMINER	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.	

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Smith *et al.*

Appl. No.: 10/661,819

Filed: September 15, 2003

For: **Thermostable Reverse  
Transcriptases and Uses Thereof**

Confirmation No.: 7510

Art Unit: 1651

Examiner: *To Be Assigned*

Atty. Docket: 0942.5040003/RWE/HCC

**Third Supplemental Information Disclosure Statement**

**Under 37 C.F.R. § 1.97(b)**

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. The numbering on this Third Supplemental Information Disclosure Statement is a continuation of the numbering in Applicants' Second Supplemental Information Disclosure Statement filed herewith in connection with the above-captioned application. Copies of the documents are provided.

Applicants' would like to bring to the Examiner's attention cited Office Actions (Documents AT16-AR18) from the following copending application, which is directed to related technical matter:

U.S. Patent Application No. 09/808,124, filed March 15, 2001.

The identification of this Office Action is not to be construed as a waiver of secrecy as to the corresponding application now or upon issuance of the present

application as a patent. The Examiner is respectfully requested to consider the cited Office Actions during prosecution of this application.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

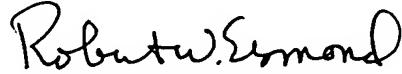
This Information Disclosure Statement is being filed before the mailing of an Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Robert W. Esmond  
Attorney for Applicants  
Registration No. 32,893

Date: Sept. 27, 2004

1100 New York Avenue, N.W.  
Washington, D.C. 20005-3934  
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FORM PTO-1449

THIRD SUPPLEMENTAL INFORMATION DISCLOSURE  
STATEMENTATTY. DOCKET NO.  
0942.5040003/RWE/HCCAPPLICATION NO.  
10/661,819FIRST NAMED INVENTOR  
*Smith et al.*FILING DATE  
September 15, 2003ART UNIT  
1651**U.S. PATENT DOCUMENTS**

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
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	AJ						
	AK						

**FOREIGN PATENT DOCUMENTS**

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM16	WO 01/68895 A1	09/20/2001	WIPO			Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

**OTHER (Including Author, Title, Date, Pertinent Pages, etc.)**

	AR		
	AS	16	Pfeiffer, J.K., et al., "Structure-Based Moloney Murine Leukemia Virus Reverse Transcriptase Mutants with Altered Intracellular Direct-Repeat Deletion Frequencies," <i>J. Virol.</i> 74:9629-9636, American Society for Microbiology (October 2000)
	AT	16	Copy of January 4, 2002, Office Action for U.S. Patent Application No. 09/808,124, Potter et al., filed March 15, 2001

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449  THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO. 0942.5040003/RWE/HCC	APPLICATION NO. 10/661,819
		FIRST NAMED INVENTOR Smith et al.	
		FILING DATE September 15, 2003	ART UNIT 1651

**U.S. PATENT DOCUMENTS**

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**FOREIGN PATENT DOCUMENTS**

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AL						Yes No
AM						Yes No
AN						Yes No
AO						Yes No
AP						Yes No

**OTHER (Including Author, Title, Date, Pertinent Pages, etc.)**

AR	<u>17</u>	Copy of May 22, 2002, Office Action for U.S. Patent Application No. 09/808,124, Potter et al., filed March 15, 2001
AS	<u>17</u>	Copy of December 3, 2002, Office Action for U.S. Patent Application No. 09/808,124, Potter et al., filed March 15, 2001
AT	<u>17</u>	Copy of August 1, 2003, Office Action for U.S. Patent Application No. 09/808,124, Potter et al., filed March 15, 2001

EXAMINER

DATE CONSIDERED

**EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

		ATTY. DOCKET NO. 0942.5040003/RWE/HCC	APPLICATION NO. 10/661,819
FORM PTO-1449  <u>THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT</u>		FIRST NAMED INVENTOR Smith et al.	
		FILING DATE September 15, 2003	ART UNIT 1651

**U.S. PATENT DOCUMENTS**

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**FOREIGN PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
AL						Yes No
AM						Yes No
AN						Yes No
AO						Yes No
AP						Yes No

**OTHER (Including Author, Title, Date, Pertinent Pages, etc.)**

AR	<u>18</u>	Copy of February 5, 2004, Office Action for U.S. Patent Application No. 09/808,124, Potter et al., filed March 15, 2001
AS		
AT		

EXAMINER	DATE CONSIDERED
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**EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Smith *et al.*

Appl. No.: 10/661,819

Filed: September 15, 2003

For: **Thermostable Reverse  
Transcriptases and Uses Thereof**

Confirmation No.: 7510

Art Unit: 1651

Examiner: *To Be Assigned*

Atty. Docket: 0942.5040003/RWE/HCC

**Fourth Supplemental Information Disclosure Statement**

**Under 37 C.F.R. § 1.97(b)**

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. The numbering on this Fourth Supplemental Information Disclosure Statement is a continuation of the numbering in Applicants' Third Supplemental Information Disclosure Statement filed herewith in connection with the above-captioned application.

No copies of U.S. patents and patent application publications cited on the attached Form PTO-1449, documents AH1 to AJ1, are submitted in accordance with 1276 OG 55 because this application was filed after June 30, 2003. Copies of documents **AS18, AT18, and AR19** are provided.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

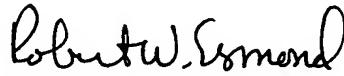
This Information Disclosure Statement is being filed before the mailing of an Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

  
Robert W. Esmond  
Attorney for Applicants  
Registration No. 32,893

Date: Sept. 27, 2004

1100 New York Avenue, N.W.  
Washington, D.C. 20005-3934  
(202) 371-2600

FORM PTO-1449

FOURTH SUPPLEMENTAL INFORMATION DISCLOSURE  
STATEMENTATTY. DOCKET NO.  
0942.5040003/RWE/HCCAPPLICATION NO.  
10/661,819FIRST NAMED INVENTOR  
Smith *et al.*FILING DATE  
September 15, 2003ART UNIT  
1651

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH1	2002/0090618 A1	07/11/2002	Smith <i>et al.</i>			05/01/2001
	AI1	2002/0119461 A1	08/29/2002	Chatterjee, D.K.			07/12/2001
	AJ1	2003/0003452 A1	01/02/2003	Potter <i>et al.</i>			03/15/2001
	AK						

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR		
	AS	18	Blain, S.W. and Goff, S.P., "Nuclease Activities of Moloney Murine Leukemia Virus Reverse Transcriptase," <i>J. Biol. Chem.</i> 268:23585-23592, The American Society for Biochemistry and Molecular Biology, Inc. (1993)
	AT	18	Lawyer, F.C., <i>et al.</i> , "Isolation, Characterization, and Expression in <i>Escherichia coli</i> of the DNA Polymerase Gene from <i>Thermus aquaticus</i> ," <i>J. Biol. Chem.</i> 264:6427-6437, The American Society for Biochemistry and Molecular Biology, Inc. (1989)

EXAMINER

DATE CONSIDERED

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FORM PTO-1449  FOURTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO. 0942.5040003/RWE/HCC	APPLICATION NO. 10/661,819
		FIRST NAMED INVENTOR Smith et al.	
		FILING DATE September 15, 2003	ART UNIT 1651

**U.S. PATENT DOCUMENTS**

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

**OTHER (Including Author, Title, Date, Pertinent Pages, etc.)**

AR	<u>19</u>	Li, W.-B., et al., "The Rapid Isolation of Specific Genes from cDNA Libraries with the GeneTrapper™ cDNA Positive Selection System," Focus 17:45-49, Life Technologies, Inc. (1995)
AS		
AT		

EXAMINER	DATE CONSIDERED
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.